Rucaparib camsylate

Cat. No.: HY-102003A

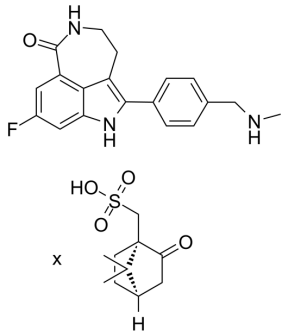
CAS No.: 1327258-57-0

Molecular Formula: $C_{19}H_{18}FN_3O.xC_{10}H_{16}O_4S$

Target: PARP

Pathway: Cell Cycle/DNA Damage; Epigenetics

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

Rucaparib (AG014699) camsylate is an orally active, potent inhibitor of PARP proteins (PARP-1, PARP-2 and PARP-3) with a K_i of 1.4 nM for PARP1. Rucaparib camsylate is a modest hexose-6-phosphate dehydrogenase (H6PD) inhibitor. Rucaparib camsylate has the potential for castration-resistant prostate cancer (CRPC) research[1][2][3][4].

IC_{50} & Target

PARP-1	PARP-2	PARP-3
1.4 nM (Ki)		

In Vitro

Rucaparib (AG014699) camsylate is a possible N-demethylation metabolite of AG14644[1].

Rucaparib (0.1, 1, 10, 100 μM; 24 hours) camsylate is cytotoxic and has the LC_{50} being 5 μM in Capan-1 (BRCA2 mutant) cells and only 100 nM in MX-1 (BRCA1 mutant) cells[2].

The radio-sensitization by Rucaparib camsylate is due to downstream inhibition of activation of NF-κB, and is independent of SSB repair inhibition. Rucaparib camsylate can target NF-κB activated by DNA damage and overcome toxicity observed with classical NF-κB inhibitors without compromising other vital inflammatory functions[5].

Rucaparib camsylate inhibits PARP-1 activity by 97.1% at a concentration of 1 μM in permeabilised D283Med cells[6].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Rucaparib (AG014699) camsylate and AG14584 significantly increase Temozolomide toxicity. Rucaparib (1 mg/kg) camsylate significantly increases Temozolomide-induced body weight loss. Rucaparib (0.1 mg/kg) camsylate results in a 50% increase in the temozolomide-induced tumor growth delay[1].

Rucaparib (10 mg/kg for i.p. or 50, 150 mg/kg for p.o.; daily for 5 days per week for 6 weeks) camsylate significantly inhibits the growth of the tumor, and there is one complete tumor regression and two persistent partial regressions[2].

Rucaparib (150 mg/kg; p.o.; once per week for 6 weeks or three times per week for 6 weeks) camsylate has greatest antitumor effect with three complete regressions[2].

Rucaparib camsylate enhances the antitumor activity of temozolomide and indicates complete and sustained tumor regression in NB1691 and SHSY5Y xenografts[6].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female CD-1 nude mice aged 10-12 weeks with Capan-1 cells[2]
Dosage:	10 mg/kg or 50, 150 mg/kg
Administration:	10 mg/kg for i.p. or 50, 150 mg/kg for p.o.

Result:	Significantly inhibited the growth of the tumor.

CUSTOMER VALIDATION

- J Med Chem. 2023 Mar 6.
- J Mol Med (Berl). 2019 Aug;97(8):1183-1193.

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REFERENCES

[1]. Thomas HD, et al. Preclinical selection of a novel poly(ADP-ribose) polymerase inhibitor for clinical trial. Mol Cancer Ther, 2007, 6(3), 945-956.

[2]. J Murray, et al. Tumour cell retention of rucaparib, sustained PARP inhibition and efficacy of weekly as well as daily schedules. Br J Cancer. 2014 Apr 15;110(8):1977-84.

[3]. Matt Shirley, et al. Rucaparib: A Review in Ovarian Cancer. Target Oncol. 2019 Apr;14(2):237-246.

[4]. Jianneng Li, et al. Hexose-6-phosphate dehydrogenase blockade reverses prostate cancer drug resistance in xenograft models by glucocorticoid inactivation. Sci Transl Med. 2021 May 26;13(595):eabe8226.

[5]. Hunter JE, et al. NF-κB mediates radio-sensitization by the PARP-1 inhibitor, AG-014699. Oncogene, 2012, 31(2), 251-264.

[6]. Daniel RA, et al. Inhibition of poly(ADP-ribose) polymerase-1 enhances temozolomide and topotecan activity against childhood neuroblastoma. Clin Cancer Res, 2009, 15(4), 1241-1249.

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